Original Article

Comparing the efficiency of ultrasound, ketoprofen, and mucopolysaccharide polysulfate phonophoresis in the treatment of lateral epicondylitis: A randomized-controlled clinical study

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ABSTRACT

Objectives: In this study, we aimed to compare the efficiency of ultrasound, mucopolysaccharide polysulfate phonophoresis, ketoprofen phonophoresis and exercise combinations in terms of pain, functionality, disability, and strength in patients with lateral epicondylitis (LE).

Patients and methods: This prospective, parallel-group, randomized-controlled clinical study included a total of 60 patients (42 males, 18 females; mean age 38.08 years; range, 21 to 50 years) with LE between April 2016 and October 2017. The patients were equally randomized into four groups based on the time of admission to the outpatient clinic. The Visual Analog Scale (VAS), painless weight lifting, the Patient-Rated Tennis Elbow Evaluation (PRTEE), and Quick Disabilities of Arm, Shoulder and Hand (QuickDASH) were used to measure the outcomes. The measurements were performed at baseline, at the end of 10 daily sessions, and after a six-week follow-up period.

Results: The resting VAS scores in the ketoprofen phonophoresis group and lifted weights in the MPS and ketoprofen phonophoresis groups showed a significant improvement both after 10 days of treatment and at six-week follow-up visits (p<0.001). In the QuickDASH model, there was no significant improvement in the control group after 10 days of treatment (p>0.05); however, a significant improvement was observed after six weeks (p<0.001). Except for these variables, significant improvements were found in all groups for all variables at six-week follow-up (p<0.05). However, improvements were similar in all groups (p>0.05).

Conclusion: Based on our study results, for LE patients who are unable to adhere to exercise and splint use and are given a physical treatment plan, inclusion of ketoprofen and MPS phonophoresis in the treatment program may yield additional benefits in their daily living activities, functionality, and working life.

Keywords: Ketoprofen, lateral epicondylitis, mucopolysaccharide polysulfate.

Lateral epicondylitis (LE) is the most common syndrome of the elbow joint.[1] Its incidence is estimated ranging from 1 to 3%.[2] It is a disease associated with overuse of extensor carpi radialis, causing pain in the lateral elbow and forearm region. Although the role of inflammation in the pathophysiology of this condition is still controversial, it has been suggested that degenerative changes in the extensor carpi radialis brevis enthesis-supporting collateral ligaments and joint capsule cause the disease.[3]

Patients frequently experience reduced hand grip strength and disturbance in daily living activities. Clinical diagnosis is often made based on the medical history and confirmatory physical signs, i.e., pain over the lateral epicondyle produced by resisted wrist and/or middle finger extension.[4] The choice of treatment for an individual patient is often based on personal experience of the treating physician. Injections, splinting, and physical therapy modalities are the major conservative treatments.[5] The most

widely used rehabilitation modalities include immobilization, splinting, thermotherapy, ultrasound, phonophoresis, iontophoresis, laser, electrical stimulation, acupuncture, manipulation, soft tissue mobilization, friction massage, and stretching and strengthening exercises.[6]

Ultrasound has been used for many years to treat musculoskeletal disorders such as tendonitis, epicondylitis, tenosynovitis, bursitis, and osteoarthritis.[7] It produces acoustic waves through transformation of electrical energy. While passing through tissues of varying resistance levels, these waves are transformed into heat.[7] Ultrasound is also used to enhance percutaneous absorption of medications in phonophoresis applications. Anti-inflammatory (i.e., piroxicam, ibuprofen, mucopolysaccharide polysulfate [MPS], and ketoprofen) and local anesthetic agents are used in combination with phonophoresis for the treatment of inflammation and pain caused by musculoskeletal system disorders such as tenosynovitis, epicondylitis, heel pain, tendinitis, bursitis, and osteoarthritis.[8,9] Anti-inflammatory effects of MPS and ketoprofen can reduce inflammation in lateral epicondyle area, alleviating the symptoms.

To the best of our knowledge, there is no study available in literature evaluating the effects of phonophoresis application of MPS in patients with LE. In the present study, we aimed to compare the efficiency of MPS phonophoresis, ketoprofen phonophoresis, and ultrasound therapy in patients with LE.

PATIENTS AND METHODS

This prospective, parallel-group, randomized-controlled clinical study was conducted at Physical Medicine and Rehabilitation Department of Tokat State Hospital and Hitit University Erol Olçok Training and Research Hospital between April 2016 and October 2017. The study population included patients aged between 18 and 50 years who were diagnosed with LE within the past three months after the onset of the condition and who experienced pain at more than two physical examinations in the Mill's test (maximal passive flexor test for the wrist), Cozen's test (resistance test for the wrist extensor), and resistance test for the middle finger.[10] A total of 80 patients with LE were screened and 20 of these patients were excluded due to lost to follow-up. The study flow chart is shown in Figure 1. Exclusion criteria were as follows: the use
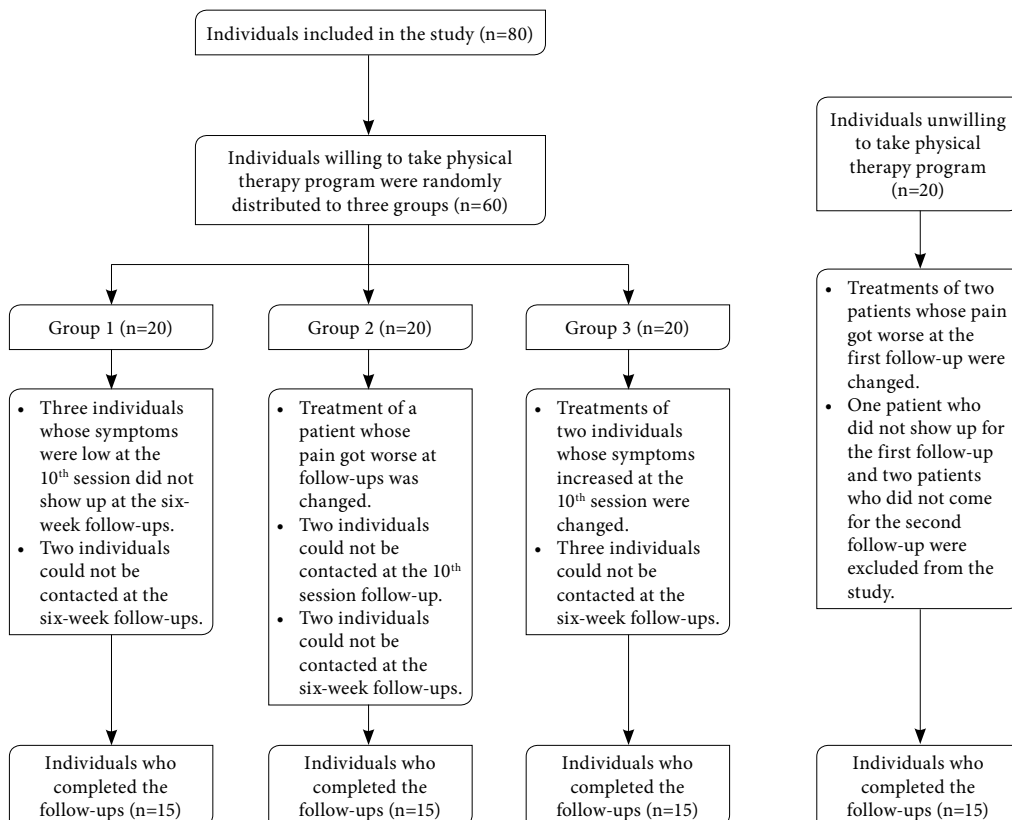

Figure 1. Study flowchart.

of corticosteroid injections involving the site within the past six months, signs and symptoms indicating causes other than overuse (e.g., cervical radiculopathy, or radial tunnel), limitation of elbow range of motion, surgery or dislocation of the elbow, tendon ruptures or fractures in the elbow area, known systemic disorders of the musculoskeletal system (e.g., osteoporosis or hemophilia,), neurological disorders (central or peripheral nervous system diseases), known malignancies, bleeding disorder, pacemaker use, and pregnancy. Finally, a total of 60 patients (42 males, 18 females; mean age 38.08 years; range, 21 to 50 years) with LE were included. A written informed consent was obtained from each patient. The study protocol was approved by the Tokat Gaziosmanpaşa University Clinical Research Ethics Committee (16-KAEK-023). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Using a stratified sampling method, the patients were randomized into four groups based on the time of admission to the outpatient clinic. Group 1 (n=15) received physical therapy consisting of hot pack for 20 min, MPS phonophoresis (1 MHz, 1.5 W/cm^2 continuous mode) for 5 min, and conventional transcutaneous electrical nerve stimulation (TENS) (100 Hz) for 30 min for a total of 10 daily sessions. Group 2 (n=15) received physical therapy consisting of hot pack for 20 min, ketoprofen phonophoresis (1 MHz, 1.5 W/cm^2 continuous mode) for 5 min, and conventional TENS (100 Hz) for 30 min for a total of 10 daily sessions. Group 3 (n=15) received general physical therapy consisting of hot pack for 20 min, ultrasound (1 MHz, 1.5 W/cm^2 continuous mode) for 5 min, and conventional TENS (100 Hz) for 30 min for a total of 10 daily sessions. Group 4 (n=15) consisted of patients who did not accept physical therapy in the hospital and received a home-based program. All groups received only paracetamol (500 mg tablet) as rescue medication for a maximum period of one week. All groups received LE exercise program and wrist rest splints for six weeks.

The outcome measures of examination findings, pain intensity, muscle strength, and functional status were evaluated at baseline, after 10 days of treatment, and six weeks after the treatment. The pain intensity was assessed using the Visual Analog Scale (VAS), for which the patient was asked to indicate his/her perceived pain during rest, activity, and pressure on the lateral epicondyle region (0-10 cm VAS, with 0 being no pain and 10 the worst imaginable pain).[11] Functional assessment of the elbow joint was performed. The Patient-Rated Tennis Elbow Evaluation (PRTEE) is a 15-item questionnaire designed to measure forearm pain and disability in patients with LE over the past week.[12] The Quick Disabilities of Arm, Shoulder and Hand (QuickDASH) Questionnaire was applied to evaluate the disability, function and pain. The QuickDASH is an abbreviated version of the original DASH outcome measure which contains 30 items, while the QuickDASH contains only 11 items.[13] The Turkish validity and reliability studies of the QuickDASH were carried out by Koldas Dogan et al. in 2011.[14] The force was assessed by determining the maximum weight (1, 2, 3 or 4 kg) which could be painlessly lifted on the affected side, when the elbow of the patient was at full extension and in the forearm pronation.[15]

Statistical analysis

Power analysis and sample size calculation were performed using the G*Power version 3.1.2 software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). Given the PRTEE variable as the primary variable, a total of 60 participants were required to be included in the study, with 15 in each group with 80% power, 5% type 1 error, and an effect size of 0.35 based on the study of Poltawski and Watson[16] Statistical analysis was performed using the IBM SPSS version 19.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were presented in mean ± standard deviation (SD) or median (min-max), while categorical variables were presented in number and frequency. The Kolmogorov-Smirnov normality test was used to evaluate the normal distribution of data. A parametric test was used, as the data were distributed normally. Two-way repeated measures analysis of variance (ANOVA) test was used to compare the groups for repeated measure variables. The Mauchly's sphericity test was used to validate a repeated measures ANOVA. The Greenhouse-Geisser method in repeated measures ANOVA was carried out where sphericity assumption was not met. The Bonferroni correction was used for post-hoc comparisons after two-way repeated measures ANOVA. The Fisher-Freeman-Halton exact test was used to compare the groups for categorical data. The internal consistency of the questionnaire was also evaluated. The Cronbach alpha (α) values over 80% were considered high reliability of questionnaires. A *p* value of <0.05 was considered statistically significant.

TABLE 1
Baseline demographic and clinical characteristic of patients

| | Groups | | | | | | | | | | | |
| | MPS (n=15) | | | Ketoprofen (n=15) | | | Ultrasound (n=15) | | | Control (n=15) | | |
Variables	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	p
Age (year)			38.8±7.5			39.1±10.5			38.3±7.7			36.1±7.2	0.758
Disease duration (month)			2.2±1.2			1.9±1.1			2.1±0.9			1.8±1.0	0.737
Sex													0.999
Female	10	66.7		11	73.3		11	73.3		10	66.7		
Male	5	33.3		4	26.7		4	26.7		5	33.3		
Dominant side													0.999
Right	14	93.3		15	100		14	93.3		15	100		
Left	1	6.7		0	0		1	6.7		0	0		
Affected side													0.928
Right	11	73.3		9	60		10	66.7		11	73.3		
Left	4	26.7		6	40		5	33.3		4	26.7		

MPS: Mucopolysaccharide polysulfate; SD: Standard deviation; Independent samples t-test or chi-square test were used.

RESULTS

A total of 60 patients completed the six-week follow-up. Of the patients, 51.7% were homemakers, 15% were civil servants, 11.7% were cleaning staff, and 6.7% were construction workers. There was no significant difference in the baseline demographic characteristics among the groups (Table 1). Baseline evaluation was not different among groups for any of these variables, except for the Mill's test which revealed a higher positivity in ketoprofen phonophoresis and control groups (p=0.002). The internal consistency of the questionnaires was assessed using the Cronbach-α value (Table 2).

For resting VAS scores in the ultrasound group, there was no significant difference between the measurements at baseline and after six weeks (p>0.05). However, the MPS and control groups showed an improvement in the resting VAS scores after 10 days of treatment compared to baseline, although the difference between the 10-day and six-week values was not significant (p>0.05). Pressure and activity VAS scores improved significantly in all groups (p<0.001). The lifted weights in MPS and ketoprofen phonophoresis groups showed a significant improvement both after 10 days of treatment and at six-week follow-up examination (p<0.001). There was no significant difference in the PRTEE scores and QuickDASH scores of the ultrasound group after 10 days of treatments, while a significant improvement was observed at six-week follow-up examination (p<0.01). In the QuickDASH model, no significant improvement was observed in the control group after 10 days of treatment (p>0.05), while a significant improvement was observed after six weeks (p<0.001). In addition, a significant improvement was also found in all groups for all other variables (p<0.05). However, in terms of improvements after six weeks of follow-up, compared to baseline values, similar results were obtained in all groups (p>0.05) (Table 3). A significant difference was found between the baseline and after six weeks in the Thomsen's, Mill's, and Maudley's tests in all groups (p<0.05), except for the Mill's test in the ultrasound group.

TABLE 2
Cronbach alpha values for questionnaires

Questionnaires	First measurement	Second measurement	Third measurement
PRTEE pain with 5 items	0.821	0.850	0.911
PRTEE function with 10 items	0.929	0.926	0.969
Quick DASH with 11 items	0.850	0.857	0.911
Quick DASH work model with 4 items	0.972	0.967	0.990

PRTEE: Patient-Rated Tennis Elbow Evaluation; DASH: Disabilities of the arm, shoulder and hand.

TABLE 3
Distribution of repeated quantitative measures according to patient groups

Variables	Groups MPS	Ketoprofen	Ultrasound	Control	$p^{\star}$
Resting VAS baseline	4.9±3.0[a]	4.7±3.2[a]	3.1±2.3[a]	4.5±3.0[a]	0.352
Resting VAS 10th day	2.5±2.8[b]	2.3±2.3[b]	1.1±1.6[b]	2.8±2.5[b]	0.243
Resting VAS 6 weeks	1.5±2.6[b]	0.4±0.8[c]	1.3±2.6a[b]	1.1±1.7[b]	0.505
$p^{\dagger}$	<0.001	<0.001	<0.001	<0.001	
	p‡=0.272; Power for interaction=0.447				
Pressure VAS baseline	7.6±2.2[a]	8.1±1.4[a]	7.5±1.9[a]	7.6±1.5[a]	0.798
Pressure VAS 10th day	4.8±1.7[b]	4.9±2.5[b]	4.4±2.8[b]	4.7±1.9[b]	0.946
Pressure VAS 6 weeks	2.9±3.0[c]	2.9±2.7[c]	2.5±3.0[c]	2.5±1.9[c]	0.963
$p^{\dagger}$	<0.001	<0.001	<0.001	<0.001	
	p‡=0.997; Power for interaction=0.065				
Activity VAS baseline	7.9±1.8[a]	8.2±1.7[a]	7.3±2.3[a]	8.3±1.4[a]	0.453
Activity VAS 10th day	5.7±2.4[b]	5.3±2.0[b]	4.5±2.4[b]	5.1±1.6[b]	0.524
Activity VAS 6 weeks	2.7±2.9[c]	2.8±2.7[c]	3.1±3.3[c]	2.1±2.0[c]	0.759
$p^{\dagger}$	<0.001	<0.001	<0.001	<0.001	
	p‡=0.341; Power for interaction=0.393				
Lifted weight baseline	2.0±1.3[a]	1.6±0.9[a]	1.8±1.3[a]	2.1±1.3[a]	0.727
Lifted weight 10th day	2.8±1.3[b]	2.6±1.4[b]	3.5±1.6[b]	2.9±1.4[b]	0.370
Lifted weight 6 weeks	4.1±1.3[c]	3.7±1.5[c]	4.1±1.8[b]	3.9±1.5[b]	0.849
$p^{\dagger}$	<0.001	<0.001	<0.001	<0.001	
	p‡=0.577; Power for interaction=0.271				
PRTEE baseline	57.2±17.3[a]	64.8±20.0[a]	55.4±11.1[a]	57.9±16.2[a]	0.427
PRTEE 10th day	35.6±16.7[b]	34.8±15.5[b]	33.8±15.0[ab]	33.2±17.7[b]	0.980
PRTEE 6 weeks	23.9±23.1[c]	18.4±16.6[c]	26.3±23.4[b]	21.3±22.4[c]	0.774
$p^{\dagger}$	<0.001	<0.001	<0.001	<0.001	
	p‡=0.354; Power for interaction=0.353				
QuickDASH baseline	46.5±17.2[a]	51.1±16.1[a]	47.1±13.1[a]	39.2±16.9[a]	0.331
QuickDASH 10th day	26.4±17.0[b]	28.3±11.5[b]	23.7±14.4[ab]	21.6±15.8[b]	0.628
QuickDASH 6 weeks	12.1±12.2[c]	9.3±10.2[c]	17.0±20.6[b]	10.9±13.9[c]	0.550
$p^{\dagger}$	<0.001	<0.001	<0.001	<0.001	
	p‡=0.325; Power for interaction=0.377				
QuickDASH work model baseline	52.6±23.0[a]	51.4±23.1[a]	51.3±22.5[a]	25.0±17.7[a]	0.116
QuickDASH work model 10th day	33.3±26.4[b]	27.1±18.2[b]	33.0±17.6[b]	8.3±10.2[a]	0.154
QuickDASH work model 6 weeks	18.3±23.5[c]	9.0±12.2[c]	23.2±26.8[b]	0±0[b]	0.151
$p^{\dagger}$	<0.001	<0.001	<0.001	<0.001	
	p‡=0.683; Power for interaction=0.205				

p* Between-subjects comparison (One-way ANOVA); p† Within-subject Comparisons (Repeated measures ANOVA); p‡: Interaction (Two-way repeated measures ANOVA); abc: In a same column for repeated measurements in each group, common subscripts indicate statistical indifference (e.g.:a-a) and different subscripts indicate statistical difference (e.g.:a-b)p p† Power was found = 1 (100%) for all repeated measures ANOVA test results.
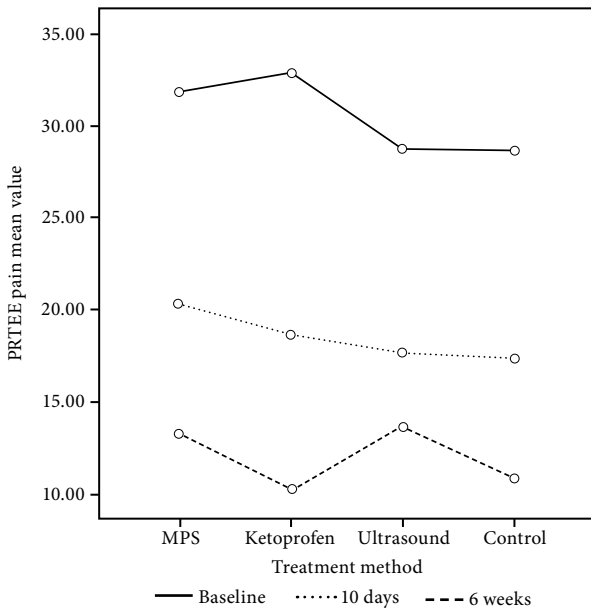
Figure 2. PRTEE pain-time-treatment method interaction.
PRTEE: Patient-Rated Tennis Elbow Evaluation.
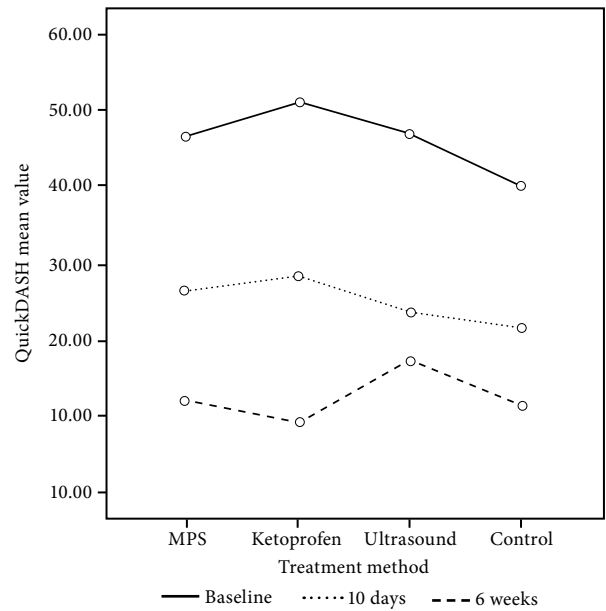
Figure 3. QuickDASH time-treatment method interaction.
QuickDASH: Quick disabilities of arm, shoulder and hand.

Although the ultrasound therapy provided a better PRTEE pain scores at six weeks, the ketoprofen and MPS phonophoresis treatment seemed to yield more favorable results in the long-term (Figure 2). All groups showed an improvement over time. The improvement in the QuickDASH score was higher in the ketoprofen phonophoresis group. However, the scores of the ultrasound group increased after 10 days (Figure 3).

DISCUSSION

Lateral epicondylitis is a common condition characterized by pain in the lateral side of the elbow with tenderness on lateral epicondyle and caused by repetitive overuse of extensor muscles of the wrist.[17] More than half of all patients with a diagnosis of LE in the present study (51.7%) were homemakers who had repetitive overuse of the hand wrist extensor muscles. In a study in which most of the individuals with LE were homemakers or teachers, 53 to 63% of the individuals were found to have stress in the hand wrist extensor muscles.[6] The presence of LE in the other occupational groups (i.e., civil servant, cleaning staff, or construction workers) in our study could be due to the long-term use of the front arm.

Physical interventions for LE have been studied by more than 200 clinical trials and have been the subject of a number of systematic reviews. The first-line treatment for LE is conservative management.[18]

In our study, significant improvements were observed in both physical treatment and control groups with splint exercises, compared to baseline. However, no significant improvement was observed in the control group after 10 days of treatment for QuickDASH model, compared to baseline. Therefore, to achieve recovery in working life and daily living activities in the acute period, physical treatment modalities should be added to exercise and splint therapies, so that individuals are able to return to work earlier. Peterson et al.[19] and Park et al.[20] compared physiotherapy and wait-and-see approaches in their studies and observed controversial findings. Peterson et al.[19] found a significant (p<0.0016) pain reduction in the treatment group, while Park et al.[20] observed significantly (p<0.01) better pain scores in the control group. Benefit from the physical therapy is not derived from the treatment itself, i.e., the physical effect of a laser therapy or the pharmacological effect of a drug. Patients also benefit from agents non-specific to treatment in a way called placebo-effect, sham-effect, or contextual effect.[21] Thus, pain relief results from the effects of treatment-specific and non-specific agents. Major non-specific agents can exert their effects as a result of expectancy, spontaneous remission, conditioning, motivation, and other psychosocial mechanisms.[21] In our study, improvements were observed in the control group for pain, disability, and functionality compared to baseline. These findings can be attributed to the home-based exercise program and

splint therapy in the control group which were used with the purpose of not leaving the patients without a treatment and to compare the efficiency of physical treatment modalities. Struijs et al.[22] evaluated the effectiveness of physical therapy, brace-only treatment, and the combination of these for patients with LE. The authors found that splint therapy was useful as an initial therapy. Furthermore, combination therapy had no additional benefits, compared to physical therapy. However, short-term combination therapy was found to be more effective than the splint therapy. Several studies have suggested that the combination of splints with physical therapy is more effective than physical therapy alone. The combined approach has been shown to yield a significant reduction in pain severity, improvement in grip strength, reduction in disability, and improvement in the ability to perform daily living activities.[22,23] The integration of particularly phonophoresis treatment into splint and exercise treatments in our study provides additional benefits both for painless weight lifting and working life activities.

External supports such as bracing/taping are also recommended for the management of LE.[18] Counterforce braces worn around the elbow work by distributing the tension on the extensor carpi radialis brevis tendon to the other areas and decreasing the tension at the site of pathology.[24] Other types of braces such as elbow straps, sleeves, and wrist splints are also available. Efficiency of these tools in alleviating the symptoms compared to placebo braces have been shown in previous studies.[24,25] In addition, the effects of proximal forearm straps and wrist extension splints on LE symptoms were compared in several studies. One study found no significant difference between the two orthotics,[26] while two others found a significant difference in favor of the wrist splint in reduction of pain.[25,27] Thus, all patients in the present study were instructed to use hand wrist splints. In a study by Clement and Chow,[23] standard physiotherapy modalities were compared to the combination of splint and physiotherapy and a significant improvement was observed in the splint + physiotherapy group for pain severity and maximum grip strength. Based on these findings, the authors emphasized the value of splint in the treatment of LE. Altan and Kanat[27] also demonstrated an improvement in pain, sensitivity to pain stimuli, algometer scores, and grip strength after a six-week wrist splint wear in patients with LE. However, there are also studies reporting that splint treatment is not superior to placebo. In a double-blinded, randomized-controlled trial conducted by Bisset et al.,[28] the immediate effects of two counterforce braces were evaluated. Thirty-four patients were tested for three conditions, i.e., forearm brace, forearm-elbow-brace, and control (no brace). All three conditions produced significant improvements for pain-free grip strength, as well as for pressure pain threshold. No significant differences were found among the brace and the control treatments. Similarly, a standard counterforce orthosis provided no immediate improvement in pain or grip strength compared to placebo in another study.[29]

It has been proposed that the exercise training alone is less effective than the combination of exercise training with electrotherapeutic modalities in the rehabilitation of LE.[30] Therefore, in our study, all groups were assigned a home-based exercise program. In a study, isometric, concentric, and eccentric exercises were found to be superior to ultrasound therapy at the end of eight weeks in terms of improvement in the grip strength and pain relief.[31] Despite the conflicting evidence, several randomize-controlled trials reported that exercise could be more effective than other treatment methods such as ultrasound, placebo or ultrasound and friction massage in reducing pain and improving function.[18] However, outcomes from various exercise types were similar.[18] Adaption to exercise could be evaluated to determine the efficiency of exercise therapy. In our study, all patients were given visual printed materials and their implementation was explained in detail. However, adherence to the program was unable to be evaluated.

In the present study, the resting VAS score improvement in the ultrasound group was lower after six weeks, compared to the evaluation after 10 days of treatment. No significant improvement was achieved after 10 days of treatment in the PRTEE and QuickDASH scores in the ultrasound group. Indeed, ultrasound group was the only group in which no significant improvement was observed from the 10 days of treatment to the six-week follow-up examination. In randomized-controlled trials, there was no significant difference in the improvement between the ultrasound therapy and placebo in the short term.[32,33] Nonetheless, a weak evidence was reported for the superiority of ultrasound therapy over placebo.[34] Since ultrasound therapy provided no additional benefit for daily living activities in LE patients with pain and limitation complaints, phonophoresis treatment could be preferred.

Ketoprofen is a drug used to alleviate inflammation and pain in clinical practice, when delivered transcutaneously.[35] Improvements were obtained for all parameters in ketoprofen phonophoresis group. In particular, for resting VAS scores after 10 days, a significant improvement was achieved only in the ketoprofen phonophoresis group. In their study, Baskurt et al.[6] compared iontophoresis and phonophoresis using naproxen and investigated the efficacy of stretching and strengthening exercises. The authors found that both treatments were equally effective in pain relief and improved grip strength.

The other phonophoresis agent used in the present study was MPS, and significant improvements were obtained for all parameters in the MPS group compared to baseline. The MPS is a naturally occurring organo-heparinoid compound. Owing to its anti-inflammatory and antithrombotic effects, this agent has been used in medicine for more than five decades in the treatment of several conditions including osteoarthritis, thrombophlebitis, and thromboembolism prophylaxis.[36] It significantly increases the levels of total and free tissue factor pathway inhibitor (TFPI), an endogenous anticoagulant and anti-inflammatory substance.[37] The TFPI increase can be observed even after topical administration of MPS. Since TFPI (local) has anti-inflammatory effects, it can be used in the treatment of superficial thrombophlebitis, hematoma, and trauma.[38] To the best of our knowledge, there is no study in the literature examining the efficiency of MPS phonophoresis for the treatment of LE. The present study is the first and, therefore, valuable. In our study, the MPS treatment yielded more favorable results than ultrasound therapy and the improvements in the PRTEE and QuickDASH scores continued after 10 days of treatment. To sustain long-term efficiency, phonophoresis treatment can be added to splint, exercise, and ultrasound therapies.

Nonetheless, there are some limitations to this study. Since the patients in the present study were in the acute phase, an improvement was observed in all groups. Thus, further studies are needed to assess the effect of treatment on patients in the chronic phase. In a study performed by Bisset and Vicenzino,[18] the patients with less than three months of pain, without an accompanying neck or arm pain, and patients whose PRTEE scores were less than 54/100 were considered to have a good prognosis. These patients were reported

to benefit from a wait-and-see approach as a result of counseling on their condition, load management including tools and workstation, and self-management within 12 weeks. Another limitation of this study is that there was no control group in the study receiving no treatment. Home-based exercises and splints were given to the control group not to leave the patients untreated. The final limitation is the lack of long-term follow-ups. The follow-up interval was intentionally chosen to determine the differences of the treatment modalities for the acute clinical outcomes in six weeks.

In conclusion, inclusion of phonophoresis in a splint treatment may be advisable to reduce the effects of the disease in daily living activities and working life. In patients with poor adherence to exercise and splinting, the addition of ketoprofen or MPS phonophoresis to the treatment plan may provide additional benefits within as early as 10 days. Besides, sustained efficiency provided by phonophoresis after 10 days of treatment can decrease hospital readmissions and reduce healthcare costs. However, further large-scale, long-term, prospective studies are needed to evaluate the exact effect of integrating MPS phonophoresis to the treatment algorithms or treatment plans for LE.

REFERENCES

1. Ciccotti MG, Charlton WP. Epicondylitis in the athlete. Clin Sports Med 2001;20:77-93.
2. Whaley AL, Baker CL. Lateral epicondylitis. Clin Sports Med 2004;23:677-91.
3. Calfee RP, Patel A, DaSilva MF, Akelman E. Management of lateral epicondylitis: current concepts. J Am Acad Orthop Surg 2008;16:19-29.
4. Raman J, MacDermid JC, Grewal R. Effectiveness of different methods of resistance exercises in lateral epicondylosis--a systematic review. J Hand Ther 2012;25:5-25.
5. Faro F, Wolf JM. Lateral epicondylitis: review and current concepts. J Hand Surg Am 2007;32:1271-9.
6. Başkurt F, Ozcan A, Algun C. Comparison of effects of phonophoresis and iontophoresis of naproxen in the treatment of lateral epicondylitis. Clin Rehabil 2003;17:96-100.
7. Klaiman MD, Shrader JA, Danoff JV, Hicks JE, Pesce WJ, Ferland J. Phonophoresis versus ultrasound in the treatment of common musculoskeletal conditions. Med Sci Sports Exerc 1998;30:1349-55.

8. Boyaci A, Tutoglu A, Boyaci N, Aridici R, Koca I. Comparison of the efficacy of ketoprofen phonophoresis, ultrasound, and short-wave diathermy in knee osteoarthritis. Rheumatol Int 2013;33:2811-8.

9. Deshpande MM, Patil CB. Heel pain and phonophoresis. J Indian Med Assoc 2010;108:365.

10. Magee DJ, editor. Orthopedic physical assessment. Philadelphia: W.B. Saunders Company; 1997.

11. Myles PS, Troedel S, Boquest M, Reeves M. The pain visual analog scale: is it linear or nonlinear? Anesth Analg 1999;89:1517-20.

12. Faes M, van den Akker B, de Lint JA, Kooloos JG, Hopman MT. Dynamic extensor brace for lateral epicondylitis. Clin Orthop Relat Res 2006;442:149-57.

13. Gummesson C, Ward MM, Atroshi I. The shortened disabilities of the arm, shoulder and hand questionnaire (QuickDASH): validity and reliability based on responses within the full-length DASH. BMC Musculoskelet Disord 2006;7:44.

14. Koldas Dogan S, Ay S, Evcik D, Baser O. Adaptation of Turkish version of the questionnaire Quick Disability of the Arm, Shoulder, and Hand (Quick DASH) in patients with carpal tunnel syndrome. Clin Rheumatol 2011;30:185-91.

15. Taşcıoğlu F, Öner C, Armağan O. The treatment of lateral epicondylitis with iontophoresis of ibuprofen and low level laser. Kocatepe Tıp Dergisi 2003;1:23-9.

16. Poltawski L, Watson T. Measuring clinically important change with the Patient-rated Tennis Elbow Evaluation. Hand Therapy 2011;16:52-7.

17. Altun RD, Incel NA, Cimen OB, Sahin G. Efficacy of ESWT for lateral epicondylitis treatment: comparison with physical therapy modalities. J Musculoskelet Res 2018;21:1850001.

18. Bisset LM, Vicenzino B. Physiotherapy management of lateral epicondylalgia. J Physiother 2015;61:174-81.

19. Peterson M, Butler S, Eriksson M, Svärdsudd K. A randomized controlled trial of exercise versus wait-list in chronic tennis elbow (lateral epicondylosis). Ups J Med Sci 2011;116:269-79.

20. Park JY, Park HK, Choi JH, Moon ES, Kim BS, Kim WS, et al. Prospective evaluation of the effectiveness of a home-based program of isometric strengthening exercises: 12-month follow-up. Clin Orthop Surg 2010;2:173-8.

21. Benedetti F, Mayberg HS, Wager TD, Stohler CS, Zubieta JK. Neurobiological mechanisms of the placebo effect. J Neurosci 2005;25:10390-402.

22. Struijs PA, Kerkhoffs GM, Assendelft WJ, Van Dijk CN. Conservative treatment of lateral epicondylitis: brace versus physical therapy or a combination of both-a randomized clinical trial. Am J Sports Med 2004;32:462-9.

23. Clements LG, Chow S. Effectiveness of a Custom-Made below Elbow Lateral Counterforce Splint in the Treatment of Lateral Epicondylitis (Tennis Elbow). Canadian Journal of Occupational Therapy 1993;60:137-44.

24. Jafarian FS, Demneh ES, Tyson SF. The immediate effect of orthotic management on grip strength of patients with lateral epicondylosis. J Orthop Sports Phys Ther 2009;39:484-9.

25. Garg R, Adamson GJ, Dawson PA, Shankwiler JA, Pink MM. A prospective randomized study comparing a forearm strap brace versus a wrist splint for the treatment of lateral epicondylitis. J Shoulder Elbow Surg 2010;19:508-12.

26. Van De Streek MD, Van Der Schans CP, De Greef MH, Postema K. The effect of a forearm/hand splint compared with an elbow band as a treatment for lateral epicondylitis. Prosthet Orthot Int 2004;28:183-9.

27. Altan L, Kanat E. Conservative treatment of lateral epicondylitis: comparison of two different orthotic devices. Clin Rheumatol 2008;27:1015-9.

28. Bisset LM, Collins NJ, Offord SS. Immediate effects of 2 types of braces on pain and grip strength in people with lateral epicondylalgia: a randomized controlled trial. J Orthop Sports Phys Ther 2014;44:120-8.

29. Wuori JL, Overend TJ, Kramer JF, MacDermid J. Strength and pain measures associated with lateral epicondylitis bracing. Arch Phys Med Rehabil 1998;79:832-7.

30. Dimitrios S. Lateral elbow tendinopathy: Evidence of physiotherapy management. World J Orthop 2016;7:463-6.

31. Pienimaki TT, Tarvainen TK, Siira PT, Vanharanta H. Progressive strengthening and stretching exercises and ultrasound for chronic lateral epicondylitis. Physiotherapy 1996;82:522-30.

32. Haker E, Lundeberg T. Pulsed ultrasound treatment in lateral epicondylalgia. Scand J Rehabil Med 1991;23:115-8.

33. Lundeberg T, Abrahamsson P, Haker E. A comparative study of continuous ultrasound, placebo ultrasound and rest in epicondylalgia. Scand J Rehabil Med 1988;20:99-101.

34. Smidt N, Assendelft WJ, Arola H, Malmivaara A, Greens S, Buchbinder R, et al. Effectiveness of physiotherapy for lateral epicondylitis: a systematic review. Ann Med 2003;35:51-62.

35. Rolf C, Engström B, Beauchard C, Jacobs LD, Le Liboux A. Intra-articular absorption and distribution of ketoprofen after topical plaster application and oral intake in 100 patients undergoing knee arthroscopy. Rheumatology (Oxford) 1999;38:564-7.

36. Wanitphakdeedecha R, Eimpunth S, Manuskiatti W. The effects of mucopolysaccharide polysulphate on hydration and elasticity of human skin. Dermatol Res Pract 2011;2011:807906.

37. Hoppensteadt DA, Fareed J, Raake P, Raake W. Endogenous release of tissue factor pathway inhibitor by topical application of an ointment containing mucopolysaccharide polysulfate to nonhuman primates. Thromb Res 2001;103:157-63.

38. Jeske W, Pifarré R, Wolf H, Fareed J. An overview of blood coagulation. In: Pifarré R, editor. New anti-coagulants for the cardiovascular patient. Philadelphia: Hanley & Belfus, Inc; 1997. p. 9-26.